PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/003972	29.03.2005	26.03.2004

International Patent Classification (IPC) or both national classification and IPC
C07K14/245, A61K39/108, C07K16/12

Applicant
MUTABILIS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Chakravarty, A Telephone No. +49 89 2399-8536

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/003972

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ not paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos.

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-28
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-28
Industrial applicability (IA)	Yes:	Claims	1-28
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item IV.

The separate inventions/groups of inventions are:

Invention 1:
Composition of SEQ ID 1 and SEQ ID 159
Invention 2-n:
Each individual embodiment has to be regarded as a separate invention, where n = number of embodiments.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

To meet the requirements of Rule. 13 PCT, for unity an inventive feature must be present which is common to all embodiments (i.e. a special technical feature).
In the present case, the different embodiments falling within claim 1 share the common alleged activity (page 4 of the description) in that they are "specific combinations of polypeptides encoded by the B2/D genome, particularly useful as antigens and can specifically prevent the pathologies due to ExPEC strains". However, this common activity or function is shared with known combinations of peptides (see e.g. WO03/0743553, paragraph 0031) and therefore cannot be regarded as a common inventive concept.
In the present case, embodiments falling within the claim can only be acknowledged as unitary if it can be shown that
i) all alternatives have a common property or activity,
and
ii) an inventive, common structural element.

As neither the first group nor the second group of polypeptides of claim 1 is defined by any fixed structural element which might be regarded as representing an inventive structural element, it follows that each individual embodiment has to be regarded as a separate invention. However, since novelty and inventive step of the "special technical feature" are already compromised by the disclosure of D1 and D2 and moreover it not technically or economically feasible to list each embodiment, in particular those pertaining to combinations of homologues of the named sequences, the search division does not intend

to require payment of additional search fees at this time.

Re Item V

1 Reference is made to the following documents:

D1 : WO 03/074553 A (ESCAICH SONIA ; MUTABILIS SA (FR)) 12 September 2003 (2003-09-12)

D2 : WO 01/21636 A (UNIV NEW YORK) 29 March 2001 (2001-03-29)

Novelty

In so far as can be assessed on the basis of the present search, the claimed subject-matter is novel. However, it should be noted that not every embodiment is covered by the search (see non-unity reasoning).

Inventive step

The claimed subject-matter lacks inventive step. The closest prior art can be seen as D1 which, as acknowledged in the description (page 6), discloses the "first group" of polypeptides, as well as combinations thereof.

The problem of "provision of alternative combinations of polypeptides for use in treatment of ExPEC *E. coli* infections" is allegedly solved by the presently claimed subject-matter.

There are two reasons why the presently claimed subject-matter cannot be regarded as inventive.

i) It was obvious to combine the polypeptides of D1 with those of D2 (which represent a different set of antigenic peptides from ExPEC *E coli*), in order to obtain a more complete coverage of antigenic regions. Since both sets of peptides and their properties were known in the art, no inventive step can be recognised for their combination. Indeed, the application only contains data showing that the combination of SEQ ID 28 and SEQ ID 159 decrease mortality of immunised mice, which result was to be expected with the sequences separately. There is no data for any other combination of named polypeptides, let alone for "homologous sequences". This leads to the second reason:

ii) no inventive step can be recognised for a large subset of the claimed subject-matter, since it is not credible that it solves the problem. This lack of credibility for arises with respect to the "homologous sequences" due to general knowledge of

structure / function relationships in the art of biological sequences, which need retain only 25% identity to the named sequence over whole of the named sequence.